

Giardiasi

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Giardiasis (popularly known as **beaver fever**)^[1] is a **zoonotic** parasitic disease caused by the **flagellate protozoan** *Giardia lamblia* (also sometimes called *Giardia intestinalis* and *Giardia duodenalis*).^[2] The giardia organism inhabits the digestive tract of a wide variety of domestic and wild animal species, as well as humans. It is the most common pathogenic parasitic infection in humans worldwide; in 2013, there were about 280 million people worldwide with symptomatic giardiasis.^[2]

1 Signs and symptoms

Symptoms include weakness in the body, **loss of appetite**, **diarrhea**, loose or watery stools, stomach cramps, upset stomach, projectile vomiting (uncommon), bloating, excessive gas, and burping (often sulfurous). Symptoms typically develop 9–15 days after exposure,^[3] but may occur as early as one day.^[4]

Symptoms are caused by Giardia organisms infecting the cells of the **duodenum** and **jejunum** of the **small intestine**^[3] and blocking nutrient absorption. Most people are asymptomatic; only about a third of infected people exhibit symptoms. If the infection is not treated, these symptoms may last for six weeks or more.

Symptomatic infections are well recognized as causing **lactose intolerance**,^[5] which, while usually temporary, may become permanent.^{[6][7]} Although **hydrogen breath tests** indicate poorer rates of carbohydrate absorption in those asymptomatically infected, such tests are not diagnostic of infection.^[8] It has been suggested that these observations are explained by symptomatic giardia infection allowing for the overgrowth of other bacteria.^{[8][9]}

Some studies have shown giardiasis should be considered as a cause of **vitamin B₁₂ deficiency** as a result of the problems caused within the intestinal absorption system.^[10]

2 Cause

Giardiasis is caused by the **protozoan** *Giardia lamblia*.^[11] The infection occurs in many animals including beavers, cows, rodents, and sheep.^[11] Animals are believed to play a role in keeping infections present in an environment.^[11]

2.1 Risk factors

According to the CDC, “those at greatest risk are travelers to countries where giardiasis is common, people in child care settings, those who are in close contact with someone who has the disease, people who swallow contaminated drinking water, backpackers or campers who drink untreated water from lakes or rivers, people who have contact with animals who have the disease, and men who have sex with men.”^[12]

It occurs more often during the summer in the United States.^[11] This is believed to be due to a greater amount of time spent on outdoor activities.^[11]

Wilderness travel within the United States is believed to be a risk factor with poorly treated or untreated water playing a role.^[11]

2.2 Transmission

Giardiasis is transmitted via the **fecal-oral route** with the ingestion of **cysts**.^[3] Primary routes are personal contact and contaminated water and food.^[3] The cysts can stay infectious for up to three months in cold water.^[11]

Not all *Giardia* infections are symptomatic, and many people can unknowingly serve as carriers of the parasite.^[13]

3 Pathophysiology

Giardia are flagellated protozoans that cause decreased expression of brush border enzymes, morphological changes to the microvillus, and programmed cell death of small intestinal epithelial cells. There is no invasion of giardia trophozoites, and small intestinal morphology may appear normal in light microscopy.

The attachment of trophozoites causes villus flattening and inhibition of enzymes that break down disaccharide sugars in the intestines. Ultimately, the community of microorganisms that lives in the intestine may overgrow and may be the cause of further symptoms, though this idea has not been fully investigated. The alteration of the villi leads to an inability of nutrient and water absorption from the intestine, resulting in diarrhea, one of the predominant symptoms. In the case of asymptomatic giardiasis, there can be malabsorption with or without histological changes to the small intestine. The degree to

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which malabsorption occurs in symptomatic and asymptomatic cases is highly varied.

The species *Giardia intestinalis* uses enzymes that break down proteins to attack the villi of the brush border and appears to increase crypt cell proliferation and crypt length of crypt cells existing on the sides of the villi. On an immunological level, activated host T lymphocytes attack endothelial cells that have been injured in order to remove the cell. This occurs after the disruption of proteins that connect brush border endothelial cells to one another. The result is heavily increased intestinal permeability.

There appears to be a further increase in programmed cell death by *Giardia intestinalis*, which further damages the intestinal barrier and increases permeability. There is significant upregulation of the programmed cell death cascade by the parasite, and, furthermore, substantial downregulation of the anti-apoptotic protein Bcl-2 and upregulation of the proapoptotic protein Bax. These connections suggest a role of caspase-dependent apoptosis in the pathogenesis of giardiasis.

Giardia protects its own growth by reducing the formation of the gas nitric oxide by consuming all local arginine, which is the amino acid necessary to make nitric oxide. Arginine starvation is known to be a cause of programmed cell death, and local removal is a strong apoptotic agent.^[14]

4 Diagnosis

- According to the CDC, detection of antigens on the surface of organisms in stool specimens is the current test of choice for diagnosis of giardiasis and provides increased sensitivity over more common microscopy techniques.^[15]

- A trichrome stain of preserved stool is another method used to detect giardia.^[16] • Microscopic examination of the stool for motile trophozoites or for the distinctive oval *G.lamblia* cysts can be performed.
- The entero-test uses a gelatin capsule with an attached thread. One end is attached to the inner aspect of the patient's cheek, and the capsule is swallowed. Later, the thread is withdrawn and shaken in saline to release trophozoites which can be detected with a microscope.
- Immunologic enzyme-linked immunosorbent assay (ELISA) testing is now available. These tests are capable of a 90% detection rate or more.^[17]
- Because *Giardia lamblia* is difficult to detect, this often leads to a delay in diagnosis or misdiagnosis; several tests should be conducted over a one-week period.^[18]

5 Prevention

The CDC recommends hand-washing and avoiding potentially contaminated food and untreated water.^[19]

Boiling suspect water for one minute is the surest method to make water safe to drink and kill disease-causing microorganisms such as *Giardia lamblia* if in doubt about whether water is infected.^[20] Chemical disinfectants or filters may be used.^{[21][22]}

According to a review of the literature from 2000, there is little evidence linking the drinking of water in the N. American wilderness and Giardia.^[23] The researcher notes that treatment of drinking water for *Giardia* may not be as important as recommended hand-washing in wilderness regions in North America.^[23] CDC surveillance data (for 2005 and 2006) reports one outbreak (6 cases) of waterborne giardiasis contracted from drinking wilderness river water in Colorado.^[24] However, less than 1% of reported giardiasis cases are associated with outbreaks.^[25]

6 Treatment

Treatment is not always necessary as the infection usually resolves on its own. However, if the illness is acute or symptoms persist and medications are needed to treat it, a nitroimidazole medication is used such as metronidazole, tinidazole, secnidazole or ornidazole.^[3]

In the US and other countries, the medication of choice used to treat giardiasis is metronidazole. In the EU a single dose of tinidazole is considered to be a first-line agent.^[26]

While tinidazole has similar side effects and efficacy to metronidazole, it is administered with a single dose.^[13]

Current research evidence suggests **albendazole** is probably as effective as metronidazole, but has fewer gastrointestinal and neurological side effects and is more convenient to take or administer.^[27] Both medications need a five to 10 day long course; albendazole is taken once a day, while metronidazole needs to be taken three times a day. A comparison of multiple drugs (**tinidazole**, **nitazoxanide**, **metronidazole**, **albendazole**) also favoured albendazole in preference to metronidazole, but did not draw any conclusions on the effectiveness of the other drugs due to a lack of reliable evidence.^[28]

In the case of nitroimidazole-resistant strains of *Giardia*, other drugs are available which have showed efficacy in treatment: **quinacrine**, **nitazoxanide**, **bacitracin zinc**, **furazolidone** and **paromomycin**.^[13]

During pregnancy, paromomycin is the preferred treatment drug because of its poor intestinal absorption.^[29]

7 Epidemiology

In some **developing countries** *Giardia* is present in 30% of the population.^[11] In the United States it is estimated that it is present in 3–7% of the population.^[11]

8 Research

Some intestinal parasitic infections may play a role in **irritable bowel syndrome**.^[30]